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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,459	11/07/2001	David L. Lewis	Mirus.030.03	3774
25032	7590	01/29/2007		
MIRUS CORPORATION 505 SOUTH ROSA RD MADISON, WI 53719			EXAMINER GIBBS, TERRA C	
			ART UNIT	PAPER NUMBER
			1635	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/29/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/007,459

Applicant(s)

LEWIS ET AL.

Examiner

Terra C. Gibbs

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2006 and 06 November 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11 and 13-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11 and 13-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed October 20, 2006 and Applicant's Terminal Disclaimer filed November 6, 2006.

Claims 11, 14, and 18 have been amended.

Claims 11 and 13-18 are pending in the instant application.

Claims 11 and 13-18 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Terminal Disclaimer

Applicant's terminal disclaimer filed November 6, 2006 is acknowledged. It is noted that the terminal disclaimer is in compliance with 37 CFR 1.321(c) or 1.321(d) and has been approved by the Patent Office and placed in the file.

Double Patenting

In the previous Office Action mailed July 25, 2006, claims 11 and 13-17 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 7 of copending Application No. 10/186,757. **This rejection is withdrawn** in view of Applicant's terminal disclaimer filed November 6, 2006.

Claim Rejections - 35 USC § 112

In the previous Office Action mailed July 25, 2006, claim 18 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is withdrawn** in view of Applicant's Amendment to the claims filed November 2, 2006. Specifically, the Examiner is withdrawing this rejection in view of Applicant's Amendment to claim 18 to correct for the lack in antecedent basis.

Claim Rejections - 35 USC § 102

In the previous Office Action mailed July 25, 2006, claims 11, 13, 14, 15, and 17 were rejected under 35 U.S.C. 102(b) as being anticipated by Sioud et al. (Nature Biotechnology, 1998 Vol. 16:556-561). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed July 25, 2006.

Response to Arguments

In response to this rejection, Applicants argue that claim 1 clearly states that the complex is inserted into a vessel. Applicants contend that Sioud et al. teaches injection into the center of a tumor.

Applicant's argument and contention have been fully considered, but are not found persuasive. First, the Examiner would like to note that claim 1 has been canceled. Therefore, despite Applicant's arguments, claim 11, not claim 1, states that the complex is inserted into a vessel.

Second, the issue is that the instant specification does not define the terms, "target tissue" and "vessel". Therefore, consistent with MPEP § 2111-2116.01, the claims have been given their broadest reasonable interpretation. In this instance, the Examiner is reasonably defining the term "target tissue" to include any tissue, but more specifically the injection site. Regarding the term "vessel", the Examiner is reasonably defining this term to include veins, arteries, or capillaries within the target tissue.

Sioud et al. disclose the direct injection of PKC α ribozymes into the center of glioma tumors in rats. Given the interpretations above, the "target tissue" is the glioma tumor itself and the "vessel" or "vessels" are veins, arteries, or capillaries within the glioma tumor.

Therefore, Sioud et al. anticipate claims 11, 13, 14, 15, and 17.

In the previous Office Action mailed July 25, 2006, claims 11, 13, 14, and 17 were rejected under 35 U.S.C. 102(b) as being anticipated by Czubayko et al. (Proc. Natl. Acad. Sci., 1996 Vol. 93:14753-14758). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed July 25, 2006.

Response to Arguments

In response to this rejection, Applicants argue that claim 1 clearly states that the complex is inserted into a vessel in a mammal. Applicants contend that Czubayko et al. teaches transfection of the ribozyme into cells *in vitro* and then insertion of the cells into mice *in vivo*.

Applicant's argument and assertion have been fully considered, but are not found persuasive. First, the Examiner would like to note that claim 1 has been canceled. Therefore, despite Applicant's arguments, claim 11, not claim 1, states that the complex is inserted into a vessel in a mammal.

Second, the Examiner agrees that Czubayko et al. teaches transfection of the ribozyme into cells *in vitro* and then insertion of the cells into mice *in vivo*. However, the claims recite, "comprising", which is open-ended language. For more explanation, see MPEP 2111.03 where it states, "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps". Therefore, the claims do not exclude the transfection of the ribozyme into cells *in vitro* and then insertion of the cells into mice *in vivo* as taught by Czybayko et al.

Third, the instant specification does not define the terms, "target tissue" and "vessel". Therefore, consistent with MPEP § 2111-2116.01, the claims have been given their broadest reasonable interpretation. In this instance, the Examiner is reasonably defining the term "target tissue" to include any tissue, but more specifically the injection site. Regarding the term "vessel", the Examiner is reasonably defining this term to include veins, arteries, or capillaries within the target tissue.

Czybayko et al. discloses the transfection of PTN ribozymes into melanoma cells *in vitro* and then the injection of these cells into subcutaneous sites on the flanks of nude mice. Given the interpretations above, the "target tissue" is the mouse flank itself and the "vessel" or "vessels" are veins, arteries, or capillaries within flank.

Therefore, Czybayko et al. anticipate claims 11, 13, 14, and 17.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed July 25, 2006, claims 11 and 13-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmer, A. (Methods, 1999 Vol. 18:286-295, made of record in the previous Office Action mailed August 24, 2005) in view of Vaish et al. (Nucleic Acids Research, 1998 Vol. 26:5237-5242), and Zhang et al. (Human Gene Therapy, 1999 Vol. 10:1735-1737, made of record in the previous Office Action mailed August 24, 2005). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed July 25, 2006.

Response to Arguments

In response to this rejection, Applicants argue claim 11 has been amended to recite the term "parenchymal cell". Applicants contend that the specification teaches that a parenchymal cell is a distinguishing cell of a gland or organ and often excludes cells that are common to many organs, specifically endothelial cells of blood vessels. Applicants point the Examiner to page 3, lines 12 and 13 and page 4, lines 8-25. Applicants also argue that the Examiner's interpretation of an efferent target tissue as a tail vein is remised since the instant application teaches that efferent blood vessels are defined as vessels in which blood flows away from the organ or tissue under normal physiologic conditions. Applicants point the Examiner to page 3, line 27 to page 4, line

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2. Applicants contend that the tail vein is an afferent blood vessel of the liver because blood flows through the tail vein to the liver.

Applicant's arguments and contentions have been fully considered. The Examiner is acknowledging that the instant claims have been amended to recite "parenchymal cell" where the instant specification teaches that a parenchymal cell is a distinguishing cell of a gland or organ and often excludes cells that are common to many organs, specifically endothelial cells of blood vessels. Also, the Examiner is acknowledging that the tail vein would be considered by the skilled artisan to be an afferent blood vessel of the liver because blood flows through the tail vein to the liver. It is noted however, that the claims recite both "afferent" and "efferent" mammalian vessels. Therefore, this argument does not obviate the instant rejection of record.

Applicants also argue that the previous Office Action mailed July 25, 2006, stated that the injection site represented a site of increased permeability where Zimmer do not teach injecting nanoparticles into the tail vein or delivery particles to the tail vein. Applicants argue that therefore, Zimmer does not teach increasing permeability of blood vessels in the target tissue.

These arguments have been fully considered, but are not found persuasive because Zimmer clearly teach injecting nanoparticles into the tail vein. For example, Zimmer teach, "Male OF1 mice (5 weeks) received a ³³P-labeled pdT₁₆ ODN bound to nanoparticles as well as an unbound control solution in the tail vein; 5 nmol/5 ml/kg was administered corresponding to 5 mg/kg nanoparticle" (see page 292, first full paragraph).

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Applicants also argue that using the Examiner's reasoning, the site of injection would represent increased permeability in a single vessel, where Step (b) of Applicant's claim 11 clearly states that permeability is increased in vessels in the target tissue.

This argument has been fully considered but is not found persuasive. The issue is that the instant specification does not define the term, "vessel". Therefore, consistent with MPEP § 2111-2116.01, the claims have been given their broadest reasonable interpretation. In this instance, the Examiner is reasonably defining the term "vessel", to include arteries, arterioles, capillaries, venules, sinusoids, veins, etc. within the tail tissue (e.g. afferent target tissue). It is noted and reiterated that delivery to the tail vein would increase permeability in the arteries, arterioles, capillaries, venules, sinusoids, veins, etc. (e.g. vessels) of the tail tissue (e.g. afferent target tissue).

Applicants further argue that claim 11 has been amended to recite, "'rapidly' inserting the complex, 'in a large volume' into an efferent or afferent mammalian vessel". Applicants contend that these amendments further differentiate Applicant's invention from the process taught by Zimmer.

This argument and contention have been fully considered, but are not found persuasive because contrary to Applicant's arguments, claim 11 has not been amended to recite, "'rapidly' inserting the complex, 'in a large volume' into an efferent or afferent mammalian vessel". In fact the terms, "rapidly" or "large volume" are not found in claim 11 or any other claim of record.

Thus, it is maintained that the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

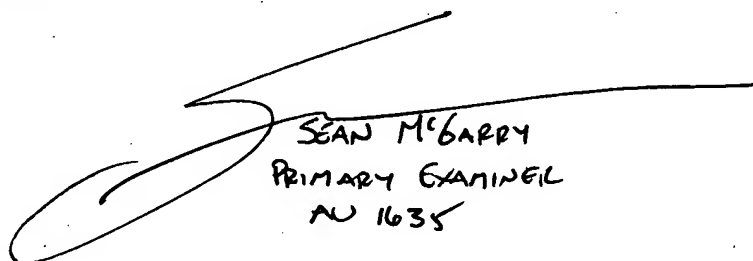
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tcg

January 18, 2007



SEAN MCGARRY
PRIMARY EXAMINER
AU 1635